A Novel, Robust and Comprehensive Predictive Tool Using Human Disease-Specific Induced Pluripotent Stem Cells for Preclinical Drug Screening

Grant Award Details

A Novel, Robust and Comprehensive Predictive Tool Using Human Disease-Specific Induced Pluripotent Stem Cells for Preclinical Drug Screening

Grant Type:	Tool Translational Research Projects
Grant Number:	TRAN4-09884
Project Objective:	**Preclinical drug screening kit with some feedback from beta testing.**

Final kit (tool) to contain:

- 100 vials cryopreserved iPSC-CMs for testing up to X drugs, representing (10 patients each of HCM, DCM, LQT and 10 healthy controls)

- phenotype reference card for given lot of CMs

- 50 96-well MEA plates

- 2 bottles customized CDM3 medium

- expiration date (at least 1 year from date of shipping if stored appropriately)

- user's manual with detailed SOPs for each step

Investigator:

Name:	Joseph Wu
Institution:	Stanford University
Type:	PI

Disease Focus:	Toxicity, Heart Disease
Human Stem Cell Use:	iPS Cell
Cell Line Generation:	iPS Cell
Award Value:	$1,000,000
Status:	Active

Grant Application Details

| **Application Title:** | A Novel, Robust and Comprehensive Predictive Tool Using Human Disease-Specific Induced Pluripotent Stem Cells for Preclinical Drug Screening |

Public Abstract:

Translational Candidate

A library of induced pluripotent stem cell-derived cardiomyocytes from healthy subjects as well as patients with common hereditary cardiac disorders

Area of Impact

Preclinical toxicity screening and drug discovery

Mechanism of Action

Patients with pre-existing cardiac conditions are more susceptible to drug-induced cardiotoxicity than general population. Including iPSCs derived from this subset of patients along with control iPSC-CMs in an in vitro assay will likely represent the heterogeneity of random population in a clinical trial and will help titrate the threshold for cardiotoxicity in high-risk patients.

Unmet Medical Need

The current preclinical assays are suboptimal and lead to elimination of many potentially promising candidates . Use of this industry-standard patient-specific iPSC-CM library will help accelerate clinical trials by accurate prediction of proarrhythmic liability in high-risk population

Project Objective

Readiness for transfer to manufacturing

Major Proposed Activities

- Generation of iPSC-CMs from 40 patients with diverse genetic and disease background.
- Detailed molecular and functional characterization of iPSC-CMs using immunofluorescence, patch clamp, calcium imaging, and other tools.
- Validation of iPSC-CMs using a panel of high, intermediate, and low risk proarrhythmic drugs by high throughput multielectrode array (MEA).

Statement of Benefit to California: California has many pharmaceutical and biotech companies. Currently, a major challenge faced by these companies is the increasing rate of drug withdrawal from market due to unpredictable cardiotoxicity, which is largely due to inefficient screening assays. The proposed predictive tool comprising of human iPSC-CMs from patients with diverse genetic background will revolutionize drug toxicity screening by accurately predicting cardiotoxicity in clinical trials and will reduce the overall cost.